Alpha-Iduronidase Enzyme Activity - Mucopolysaccharidosis Type I

Disease Overview

Mucopolysaccharidosis type I (MPS I) is a progressive disorder that ranges in severity and can affect numerous systems throughout the body. Subtypes include attenuated MPS I (previously known as Hurler-Scheie and Scheie syndromes) and severe MPS I (formerly Hurler syndrome). Symptoms vary widely but can include cardiomyopathy, "coarse" facial features (eg, thickening of the earlobes, lips, outside of nostrils, and tongue), intellectual disability, organomegaly, and progressive skeletal dysplasia.[1]

Genetics

Gene

IDUA

Inheritance

Autosomal recessive

Incidence

MPS I: ~1/70,000

- Attenuated MPS I: 1/500,000[1]
- Severe MPS I: 1/100,000[1]

Genotype/Phenotype Correlation

MPS I Subtype	Characteristics
Attenuated MPS I	Variants are often milder (eg, single base-pair substitutions) • Some residual enzyme function is retained
Severe MPS I	Associated with more severe, nonsense variants • Profound alpha-iduronidase deficiency

Test Interpretation

Results

An extremely low or undetectable level of alpha-iduronidase enzyme activity in leukocytes is consistent with MPS I.

Limitations

Testing for alpha-iduronidase enzyme activity:

- Cannot differentiate between attenuated MPS I (ie, Hurler-Scheie and Scheie syndromes) and severe MPS I (Hurler syndrome)
  - Categorization depends on clinical and/or molecular genetic findings
- Cannot predict carrier status for MPS I
- Does not evaluate enzyme deficiencies in other MPS types

Featured ARUP Testing

Screening

Mucopolysaccharides Screen - Electrophoresis and Quantitation, Urine 0081352

Method: Electrophoresis/Spectrophotometry

Recommended initial test to screen for all mucopolysaccharidosis types, including MPS I

Diagnosis/Monitoring

Alpha-Iduronidase Enzyme Activity in Leukocytes 2011415

Method: Quantitative Fluorometry

Recommended test to exclude MPS I following an abnormal screen or to confirm MPS I in patients with a consistent clinical phenotype and/or a positive family history

Mucopolysaccharidoses Type 1/2, Total Heparan Sulfate and NRE (Sensi-Pro(R)) Quantitative, Urine 3003552

Method: Liquid Chromatography-Tandem Mass Spectrometry

Use to confirm a diagnosis of MPS I or to monitor glycosaminoglycan (GAG) levels in patients with confirmed MPS I

Mucopolysaccharidoses Type 1/2, Total Heparan Sulfate and NRE (Sensi-Pro(R)) Quantitative, Serum or Plasma 3003566

Method: Liquid Chromatography-Tandem Mass Spectrometry

Use to confirm a diagnosis of MPS I or to monitor GAG levels in patients with confirmed MPS I

Mucopolysaccharides, Quantitative, Urine 0081357

Method: Spectrophotometry

Use to monitor GAG levels in patients with confirmed MPS I

Additionally, pseudodeficiency has been demonstrated for this enzyme due to specific gene variants that affect the exogenous substrate but not endogenous substrates. Individuals with pseudodeficiency are not affected with MPS I.

References

1. Clarke LA. Mucopolysaccharidosis type I. In: Adam MP, Ardinger HH, Pagon RA, et al., eds. GeneReviews, University of Washington, Seattle; 1993-2022. [Last update: Feb 2021; Accessed: Jan 2022]

Additional Resources

Beck M, Arn P, Giugliani R, et al. The natural history of MPS I: global perspectives from the MPS I Registry. *Genet Med*. 2014;16(10):759-765.

Clarke LA. The mucopolysaccharidoses: a success of molecular medicine. *Expert Rev Mol Med*. 2008;10:e1.

Enns GM, Steiner RD, et al. Lysosomal disorders. In: Sarafoglou K, Hoffman GF, Roth KS, eds. *Pediatric Endocrinology and Inborn Errors of Metabolism.* McGraw-Hill Education/Medical; 2009:747-748.

Lawrence R, Brown JR, Al-Mafraji K, et al. Disease-specific non-reducing end carbohydrate biomarkers for mucopolysaccharidoses. *Nat Chem Biol*. 2012;8(2):197-204.

National Organization for Rare Disorders (NORD). Mucopolysaccharidosis type I. [Published: 2019; Accessed: Jan 2022]

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